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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,805	12/02/2003	Harold H. Schmitz	1010-133US1	3329

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NADA JAIN, P.C.
560 White Plains Road, Suite 460
Tarrytown, NY 10591

EXAMINER	
LEITH, PATRICIA A	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,805	SCHMITZ, HAROLD H.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *19-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-32 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-12 in the reply filed on 12/16/05 is acknowledged. The traversal is on the ground(s) that 'because the relationship between cytokine baseline levels and individual's responsiveness to treatment is the basis for all pending claims, prior art search with respect to any of the restriction groups would uncover art relevant to the other groups" (p. 8, Arguments. This is not found persuasive because, as indicated in the Requirement for Restriction, all of the Groups employ different method steps, thus leading to separate searches of the prior art. Because claims 13-18 and new claims 29-32 depend upon Group I, these claims are joined with Group I to be searched on the merits.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19-28 are hereby withdrawn from examination on the merits as they are directed toward a non-elected invention.

Claims 1-18 and 29-32 were examined on the merits.

Specification

The disclosure is objected to because of the following informalities: The Instant phspecification recites "The compounds for use in the present invention are flavanols, such as epicatechin, catechin and gallated forms thereof...". However, according to Harborne et al. (ed) Phytochemical dictionary, catechin is a flavonoid (see p. 411, compound 1538) which is in a different chemical class than flavanols. Thus, it is unclear what class of compounds to which Applicant is actually refering to, which thus causes ambiguity in the claims (please see claim rejection under 35 USC 112 Second paragraph *infra*).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 and 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). It appears that the term "flavanol" in the claims is used by the claim to mean compounds falling in the same class as catechin, while the accepted meaning is "flavonoids." The term is indefinite because the specification does not clearly redefine the term.

Claims 1-18 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Nowhere in the Instant specification as filed is there any indication that Applicant was in possession of designing a dietary and/or pharmaceutical regimen based upon baseline cytokine levels. There is no information of actually how to go about assessing an individual's baseline cytokine level in order to diagnose or treat a disease. Thus, the specification does not describe an actual reduction to practice by showing that the

inventor constructed an embodiment or performed a process that met all the limitations of the claims and determined that the invention would work for its intended purpose.

The MPEP states that the purpose of the written description requirement is to ensure that the invention had possession, as of the filing date of the application, of the specific subject matter later claimed by him or her. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention.' Lockwood v. American Airlines, Inc., 107 F. 3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F. 2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F. 3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F. 2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does **"little more than outline [goals] appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate**.")· emphasis added. Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the Inventor, at the time the application was filed had possession of the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the claims are not enabled because there are no enabled embodiments in the claims. However, there is an enabled embodiment found in the

Specification, which is the modulation of TGF- β by use of cocoa derived catechin and epicatechin. Therefore, although the claims are not enabled in their entirety (and a rejection supporting lack of enablement follows), if Applicant chooses to amend the claims to reflect the enabled scope which is found in the Specification, the Examiner has also indicated scope of enablement problems below.

Claims 1-18 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method for 'designing, a dietary and/or a pharmaceutical regimen', for modulating all cytokines in all cells with any flavanol or procyanidin oligomer or derivative thereof, nor does it provide enablement to diagnose or treat a disease, or to promote homeostatic cytokine levels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to

make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease conditions are relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

First, the claims recite any cytokine. There is lack of guidance in the Instant specification as filed which would indicate that procyanidins would have an effect on PBMC excretion of all cytokines, except for what is already known in the art; i.e., TGF-

β, IL-5 and IL- 1 β . It is well known that all cytokines differ with regard to structure and function and will therefore react differently in reaction to foreign stimuli. Thus, there has been no nexus established in order to verifiably conclude that cocoa proanthocyanidins will modulate the production of any other cytokines besides TGF- β, IL-5 and IL- 1 β.

Secondly, the claims are not enabled for TGF- β (or any other cytokine) modulation in all cells. The Instant specification provides guidance for one cell type only; namely, peripheral blood mononuclear cells (PBMC's). The state of the art is unpredictable with regard to the biochemistry of cytokines in cells because the exact roles of cytokines such as TGF- β have not been, to date, specifically elucidated. What is known in the art is that TGF- β plays different roles in different cells dependant upon external influences. For example, Wimmel et al. (2003) report that "It has been well documented that TGF β-1 switches from an inhibitor of tumour cell growth to a stimulator of growth and invasion during carcinogenesis in a variety of tumors. 'For example, while TGF β-1 inhibits growth in non-transformed colonocytes, it stimulates proliferation in approximately 50% of colon cancer cell lines' " (see p. 1315). Further, with regard to TNF "...on some tumor cells TNF at most exerts a 'cytostatic' activity, while some other tumor cells do not respond to TNF at all" (Beyaert et al. (1994)).

Thus, it is highly unpredictable to ascertain whether cocoa phytochemicals will have any effect on cytokine production of cells besides PMBC's and to determine if other cells will actually be effected by cocoa proanthocyanidins would entail undue

experimentation on the part of the skilled artisan without any reasonable expectation of success due to the unpredictability of cytokine biochemistry as well documented in the art.

Thirdly, the claims are not enabled for modulating TGF- β (or any other cytokine) with any flavanol, any procyanidin oligomer and any derivatives of these. It is noted that Applicant has not provided any information with regard to derivatives of flavanols or procyanidin oligomers which would have any effect on cytokine modulation in PBMC's. A 'derivative' of these compounds is broad enough to encompass a simple carbon compound or a hydroxyl group for example. Thus, the skilled artisan would have trouble practicing the invention with a 'derivative' of these compounds lacking specific guidance with regard to 'derivatives' in the Instant specification. With regard to the broadly claimed 'flavanol' and 'procyanidin oligomers', it is deemed that the Instant specification is not enabled for all flavanols and all procyanidin oligomers because the state of the art is unpredictable and the Instant specification has provided no guidance with regard to flavanols and procyanidin oligomers from any other source besides cocoa. First, it is noted that there is some ambiguity with regard to the term 'flavanol' as recited in the Instant specification and in the claims. The Instant specification recites "The compounds for use in the present invention are flavanols, such as epicatechin, catechin and gallated forms thereof...". However, according to Harborne et al. (ed) Phytochemical dictionary, catechin is a flavo*noid* (see p. 411, compound 1538). Flavonoids are a different class of compounds from flavanols (which is actually claimed)

as can be seen by their respective category in the Phytochemical dictionary. The Examiner has provided lists of both flavonoids and flavones taken from the Phytochemical dictionary (see pp. 407-457). What is clear from this reference is that flavanols, as well as flavonoids, possess different structures, are derived from vastly different plant genus/species and provide for vastly different medicinal functions. Thus, although each has a similar base structure, each flavanol/flavonoid is unique in structure and function and would not be considered obvious variants of each other. Applicant has not disclosed the usefulness of any phytochemical monomer besides catechin, which is a flavonoid. Due to the unpredictability in the art, coupled with the lack of guidance with regard to any other flavanols which would be even relatively effective in modulating cytokines in PBMC's, the skilled artisan would need to succumb to tedious trial and error protocols in order to ascertain the effectiveness of any other flavonoids/flavanols.

Fourth, Applicant claims 'regimen to promote homeostatic cytokine levels'. There is no indication in the Instant specification nor in the prior art exactly what a 'homeostatic' cytokine level is. Judging from the prior art, 'abnormal' cytokine levels can only be determined from comparison of an individual's own normal cytokine level or in comparison with another healthy subject (see for example Pierson III et al. (US 20050079176 A1) [0045] and [0335]), The Instant specification teaches that samples were taken from 13 healthy volunteers and that Applicant split these samples into two categories which they considered 'low baseline' and 'high baseline' with regard to

PBMC TGF- β excretion. Although Applicant has arbitrarily categorized these samples in this manner, there is no indication that the original baseline quantified from these samples were *not* homeostatic. It appears to be assumption in the Instant specification that providing cocoa proanthocyanidins will restore TGF- β to a 'homeostatic' level because there is no verifiable evidence which concludes that the samples which were obtained from healthy individuals were *in any way* abnormal. It is clear that some of the cocoa phytochemicals had an effect on TGF- β production; by either exciting secretion in the 'low baseline' individuals, or inhibiting TGF- β production in the 'high baseline' individuals. However, the Instant specification provides no indication that this effect actually produced homeostasis with regard to TGF- β.

Lastly, the claims are not enabled for treatment of any disease such as coronary heart disease, cardiac fibrosis, atherosclerosis and or renal disease or failure or diagnosing such a disease based upon a baseline cytokine level. The Instant specification fails to provide any information or working examples in order to ascertain if the method would be even relatively effective in treating any disease. Again, the state of the art is unpredictable with regard to modulation of cytokines and treatment of diseases. Although the level of some cytokines is taken as a marker for potential disease states, it has not been verifiably proven in the Instant specification nor in the prior art that these disease will always occur. Further, there is no indication in the Instant specification what level of TGF- β or any other cytokine baseline value would be indicative of a marker for these diseases and further if the amount of modulation which

occurred would have any effect on these diseases. In order for the skilled artisan to obtain this information, it would require time consuming, arduous trial and error protocols including collection of numerous *in-vitro* as well as clinical data.

To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve considerable undue experimentation.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, **he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art**; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (emphasis added)

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Thursday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith
Primary Examiner
Art Unit 1655

February 16, 2006